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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/775,678	02/10/2004	Kurt von Figura	S2071-702810	3614

37462 7590 05/13/2011

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EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1656	

NOTIFICATION DATE	DELIVERY MODE
05/13/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@LALaw.com
gengelson@LALaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/775,678	FIGURA ET AL.	
	Examiner	Art Unit	
	DAVID J. STEADMAN	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *86-96,101-112 and 116-123* is/are pending in the application.

4a) Of the above claim(s) *91,106 and 112* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *86-90,92-96,101-105,107-111 and 116-123* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/9/11, 4/26/11*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Appendices A,B*.

DETAILED ACTION

Status of the Application

[1] A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/9/11 has been entered.

[2] Claims 86-96, 101-112, and 116-123 are pending in the application.

[3] Applicant's amendment to the claims, filed on 2/9/11, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

[4] Receipt of information disclosure statements filed on 2/9/11 and 4/26/11, is acknowledged.

[5] Applicant's remarks filed on 2/9/11 in response to the final rejection mailed on 8/9/10 have been fully considered and are deemed to be persuasive to overcome at least one of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[6] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Election/Restriction

[7] Claims 91, 106, and 112 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

[8] Claims 86-90, 92-96, 101-105, 107-111, and 116-123 are being examined on the merits. Claims 96 and 111 are being examined only to the extent the claims read on the elected subject matter, *i.e.,* Iduronate 2-Sulfatase.

Information Disclosure Statement

[9] The information disclosure statements (IDS) submitted on 2/9/11 and 4/26/11 were filed prior to the mailing date of the instant first Office action on the merits after request for continued examination on 2/9/11. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

Claim Objection

[10] Claims 86 and 92-93 are objected to in the recitation of "a Formylglycine Generating Enzyme comprising amino acids 34-374 of SEQ ID NO:2 or SEQ ID NO:2" and in the interest of improving claim form, it is suggested that the noted phrase be amended to recite, *e.g.,* "a Formylglycine Generating Enzyme comprising the amino acid sequence of amino acids 34-374 of SEQ ID NO:2 or SEQ ID NO:2".

Claim Rejections - 35 USC § 112, Second Paragraph

[11] The rejection of claim(s) 86-90, 92-96, 101-105, 107-111, and 116-123 under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "exogenous sulfatase" and "exogenous Formylglycine generating enzyme" is withdrawn in view of the instant amendment to claims 86, 92-94, 101, 107-109, 117, 119, 121, and 123 to delete the term "exogenous".

[12] The rejection of claims 86-90, 92-96, 101-105, 107-111, and 116-123 under 35 U.S.C. 112, second paragraph, as lacking antecedent basis in the recitation of "the gene encoding the endogenous sulfatase" and "the gene encoding the endogenous Formylglycine generating enzyme" is withdrawn in view of the instant amendment to claims 86 and 101 to delete the phrases at issue.

[13] The rejection of claims 86-90, 92-96, 101-105, 107-111, and 116-123 under 35 U.S.C. 112, second paragraph, as being confusing in the recitation of "the gene encoding the endogenous...comprises a heterologous promoter upstream of an endogenous sulfatase gene genomic locus" is withdrawn in view of the instant amendment to claims 86 and 101 to delete the phrase "upstream of an endogenous...genomic locus".

[14] Claims 86-90, 92-96, 101-105, 107-111, and 116-123 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 86 (claims 87-90, 92-96, 116-117, and 120-121 dependent therefrom) and 101 (claims 102-105, 107-111, 118-119, and 122-123 dependent therefrom) are indefinite in the recitation of "A cultured cell..." because it is unclear as to the intended meaning of the term "cultured". In this case, the term "cultured" with respect to a cell can be interpreted as meaning a cell that is actively and presently in culture or in the alternative can be interpreted as meaning a cell that *was* in culture, but is no longer actively being cultured. It is suggested that applicant clarify the meaning of the noted phrase.

[15] Claim 107 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 107 is indefinite in the recitation of "a Formylglycine Generating Enzyme" because it is unclear as to whether or not the recited FGE is limited to having an amino acid sequence that comprises an amino acid sequence that has at least 95% identity to the amino acid sequence of amino acids 34-374 of SEQ ID NO:2 or SEQ ID NO:2" as recited in claim 101. It is suggested that applicant clarify the meaning of the claim.

Claim Rejections - 35 USC § 112, First Paragraph

[16] Claims 86-90, 93-96, 101-105, 108-111, and 116-123 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an *isolated* sulfatase-producing cell, does not reasonably provide enablement for all

cultured sulfatase-producing cells as broadly encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue." *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). The Factors considered to be most relevant to the instant rejection are addressed in detail below.

The nature of the invention: According to the specification, FGE is an enzyme responsible for post-translationally modifying a conserved cysteine residue in eukaryotes or a conserved serine residue in prokaryotes of a sulfatase polypeptide, yielding L-C-formylglycine, in which an aldehyde group replaces the thiomethyl group of the cysteine (p. 1, lines 20-29). The specification goes on to disclose that FGE can be used to enhance the activity of a sulfatase polypeptide (p. 3, lines 15-19).

The breadth of the claims: The claims are drawn to a "cultured" sulfatase-producing cell, wherein the ratio of active sulfatase to total sulfatase produced by the cell is increased relative to a cell without the FGE and the cell comprises:

(i) (a) an endogenous nucleic acid operably linked to a heterologous promoter, wherein the endogenous nucleic acid encodes a sulfatase, or (b) a heterologous nucleic acid, wherein the heterologous nucleic acid encodes a sulfatase; and

(ii) (a) an endogenous nucleic acid operably linked to a heterologous promoter, wherein the endogenous nucleic acid encodes an FGE comprising the amino acid sequence of SEQ ID NO:2 or the amino acid sequence of amino acids 34-374 of SEQ ID NO:2 or 95% identical variants thereof, or (b) a heterologous nucleic acid, wherein the heterologous nucleic acid encodes an FGE comprising the amino acid sequence of SEQ ID NO:2 or the amino acid sequence of amino acids 34-374 of SEQ ID NO:2 or 95% identical variants thereof,

wherein the ratio of active sulfatase to total sulfatase produced by the cell is increased by at least 5% as compared to the ratio in the same cell type without the FGE of (ii).

Regarding the term "cultured" with respect to a cell, the term "cultured" can be interpreted as meaning a cell that is actively being cultured, or, in the alternative, the term "cultured" can be interpreted as meaning a cell that was cultured, but is no longer actively being cultured. When interpreted in light of the specification's disclosure at, *e.g.,* pp. 29 and 39, the "cultured sulfatase-producing cell" is interpreted as being an

embryonic stem cell, germ line cell, and/or somatic cell that was cultured and is now within or a part of a transgenic organism.

The state of the prior art; The level of one of ordinary skill; and The level of predictability in the art: Regarding the scope of sulfatase-producing cells encompassing cells of a transgenic organism, the prior art acknowledges the unpredictability of gene transfer in an animal. See, *e.g.,* Sang (*Mechanisms of Development* 121:1179-1186, 2004).

The amount of direction provided by the inventor and The existence of working examples: The specification fails to disclose even a single working example of a cultured cell that is part of a transgenic animal and fails to provide specific guidance or direction for making such a transgenic animal.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: It was not routine in the art at the time of the invention to increase cellular expression of a sulfatase and/or FGE within a cell by producing the sulfatase and/or FGE outside of the cell, including a transgenic animal.

Thus, in view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability as evidenced by the prior art, and the amount of experimentation that is required, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention. Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a

reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

RESPONSE TO ARGUMENT: Beginning at p. 10 of the instant remarks, applicant argues the rejection is obviated by amendment to limit the claimed cell to a "cultured" cell.

Applicant's argument is not found persuasive. At least for the reasons set forth above, the examiner maintains the position that a "cultured" cell still encompasses a cell within a transgenic animal, particularly in view of the specification's disclosure.

Claim Rejections - 35 USC § 102/103

[17] Claims 86-90, 93-96, 101-105, 108-111, and 116-123 are rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Rommerskirch et al. (*Proc. Natl. Acad. Sci. USA*, 89:2561-2565, 1992; cite U of Form PTO-892 mailed on 9/17/07; hereafter "Rommerskirch") as evidenced by Eto et al. (*Eur. J. Pediatr.* 135:85-89, 1980; hereafter "Eto") and Dierks et al. (*Cell* 113:435-444, 2003; cite CS of the IDS filed on 2/28/05; hereafter "Dierks"). See MPEP 2112.III regarding a rejection under 35 U.S.C. 102/103 and see MPEP 2131.01 regarding a multiple reference rejection under 35 U.S.C. 102.

Regarding the limitation, a cultured sulfatase-producing cell, the reference of Rommerskirch teaches a metachromatic leukodystrophy (MLD) fibroblast cell infected with a retroviral gene transfer vector comprising a herpes simplex virus thymidine kinase promoter and a sulfatase-encoding nucleic acid (p. 2562, column 1 and Figure 2), where the cell produces arylsulfatase A (p. 2563, Table 1).

Regarding the limitation, the cell comprises: (i) (a) an endogenous nucleic acid operably linked to a heterologous promoter, wherein the endogenous nucleic acid encodes a sulfatase, it is noted that the recited "endogenous nucleic acid" is broadly interpreted to encompass the genomic DNA of the MLD fibroblast of Rommerskirch, which genomic DNA is considered to be operably linked to the inserted thymidine kinase promoter because the thymidine kinase promoter is active in promoting transcription of sulfatase in the MLD fibroblast. The herpes simplex thymidine kinase promoter is heterologous to the MLD fibroblast. Evidentiary reference Eto discloses that MLD fibroblasts endogenously produce sulfatase, *e.g.,* arylsulfatase B (p. 86, Table 1), and thus the modified genomic DNA of the MLD fibroblast cell of Rommerskirch necessarily encodes a sulfatase. This meets the recited limitation.

Regarding the limitation, the cell comprises: (i)...(b) a heterologous nucleic acid, wherein the heterologous nucleic acid encodes a sulfatase in claims 86 and 101, the retroviral vector sequence is heterologous to the genomic DNA of the MLD fibroblast and encodes a sulfatase. This meets the recited limitation.

Regarding the limitation, the cell comprises:...(ii) (a) an endogenous nucleic acid operably linked to a heterologous promoter in claims 86 and 101, it is noted that the

recited "endogenous nucleic acid" is broadly interpreted to encompass the genomic DNA of the MLD fibroblast of Rommerskirch, which genomic DNA is considered to be operably linked to the heterologous thymidine kinase promoter because the thymidine kinase promoter is active in promoting transcription of sulfatase in the MLD fibroblast. This meets the recited limitation.

Regarding the limitation, the cell comprises:..(ii)...(b) a heterologous nucleic acid" in claims 86 and 101, it is noted that the recited "heterologous nucleic acid" is broadly interpreted to encompass the genomic DNA with the inserted vector sequence, which is heterologous to the genomic DNA without the inserted vector sequence. This meets the recited limitation.

Regarding the limitation, wherein the endogenous nucleic acid encodes an FGE comprising the amino acid sequence of SEQ ID NO:2 or the amino acid sequence of amino acids 34-374 of SEQ ID NO:2 or 95% identical variants thereof, or (b) a heterologous nucleic acid, wherein the heterologous nucleic acid encodes an FGE comprising the amino acid sequence of SEQ ID NO:2 or the amino acid sequence of amino acids 34-374 of SEQ ID NO:2 or 95% identical variants thereof in claims 86 and 101, the evidentiary reference of Dierks discloses that human FGE (p. 437, Figure 3), which is 100% identical to SEQ ID NO:2 herein, is expressed in fibroblasts (p. 437, column 2, bottom) and the cell of Rommerskrich is a fibroblast. This meets the recited limitation.

Regarding the limitation, wherein the active sulfatase to total sulfatase produced by the cell is increased by at least 5% as compared to the ratio in the same cell type

without the FGE of (ii), the MLD fibroblasts recombinantly expressing arylsulfatase A exhibit an increase in the ratio of active sulfatase to total sulfatase of at least 100% as compared to MSD fibroblasts, where MLD fibroblasts and MSD fibroblasts are the same cell type, *i.e.,* fibroblasts, and evidentiary reference Dierks provides evidence that MSD fibroblasts are defective in FGE activity (p. 440, Table 2), *i.e.,* are without the FGE of (ii). This meets the recited limitation.

Regarding the limitation, wherein the FGE is capable of forming L-C_α-formylglycine on a sulfatase in claim 101, evidentiary reference Dierks teaches FGE catalyzes the formation of C_α-formylglycine (FGly) at the active site of eukaryotic sulfatases (p. 435, abstract). This meets the recited limitation.

This anticipates claims 86-90, 93-96, 101-105, 108-111, and 116-123 as written.

[18] Claims 101-105, 107, 119, and 123 are rejected under 35 U.S.C. 102(e) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Fraser et al. (US Patent 7,083,793 B2; hereafter "Fraser") as evidenced by Landgrebe et al. (Gene 316:47-56, 2003; hereafter "Landgrebe"), Plasmid Vectors (obtained from www.mfa.od.ua/page275.htm, last viewed on 5/9/11), and Dierks (*supra*). See MPEP 2112.III regarding a rejection under 35 U.S.C. 102/103 and see MPEP 2131.01 regarding a multiple reference rejection under 35 U.S.C. 102. This rejection is directed to the cultured sulfatase-producing cell of claims 101-105, 107, 119, and 123 being a *prokaryotic* cell.

Regarding the limitation, a cultured sulfatase-producing cell, evidentiary reference Landgrebe teaches *E. coli* carries cysteine-type sulfatase genes (p. 55, column 1, bottom).

Regarding the limitation, the cell comprises: (i) (a) an endogenous nucleic acid operably linked to a heterologous promoter, wherein the endogenous nucleic acid encodes a sulfatase, Fraser teaches a BL21(DE3) *E. coli* as a host cell for recombinant protein expression (column 48, lines 9-21). Fraser teaches BL21(DE3) carries a lacUV5 promoter (column 48, lines 19-21) and evidentiary reference Plasmid Vectors teaches lacUV5 is a mutant promote and is considered to be a "heterologous promoter". It is noted that the recited "endogenous nucleic acid" is broadly interpreted to encompass the genomic DNA of the BL21(DE3) of Fraser, which genomic DNA is considered to be operably linked to the lacUV5 promoter because the lacUV5 promoter is active in promoting transcription of T7 RNA polymerase. This meets the recited limitation.

Regarding the limitation, the cell comprises: (i)...(b) a heterologous nucleic acid, wherein the heterologous nucleic acid encodes a sulfatase in claims 86 and 101, the lacUV5 promoter is heterologous to the genomic DNA of the BL21(DE3) of Fraser and encodes a sulfatase. This meets the recited limitation.

Regarding the limitation, the cell comprises:..(ii)...(b) a heterologous nucleic acid, wherein the heterologous nucleic acid encodes an FGE comprising the amino acid sequence of amino acids 34-374 of SEQ ID NO:2 or 95% identical variants thereof in claims 86 and 101, Fraser teaches BL21(DE3) *E. coli* transformed with an expression vector encoding a polypeptide with the amino acid sequence of SEQ ID NO:15 (column

48, lines 9-21), which is 100% identical to amino acids 34-374 of SEQ ID NO:2 herein (see Appendix A sequence alignment). This meets the recited limitation.

Regarding the limitation, wherein the active sulfatase to total sulfatase produced by the cell is increased by at least 5%, 10%, 20%, 50%, or 100% as compared to the ratio in the same cell type without the FGE of (ii), although Fraser does not teach the BL21(DE3) recombinantly expressing the SEQ ID NO:15 polypeptide increases active sulfatase activity, this is a necessary characteristic of the cell of Fraser. Since the Office does not have the facilities for examining and comparing applicant's cell with the cell of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the cell of the prior art does not possess the same material structural and functional characteristics of the claimed cell). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594. This meets the recited limitation.

Regarding the limitation, wherein the FGE is capable of forming L-C_{α}-formylglycine on a sulfatase in claim 101, although Fraser does not expressly teach the polypeptide has this activity, evidentiary reference Dierks teaches FGE catalyzes the formation of C_{α}-formylglycine (FGly) at the active site of eukaryotic sulfatases (p. 435, abstract). This meets the recited limitation.

This anticipates claims 101-105, 107, 119, and 123 as written.

Claim Rejections - 35 USC § 103

[19] Claims 86-90, 92, 117, and 121 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosen et al. (US Patent 7,368,531 B2; hereafter "Rosen") in view of Fraser et al. (US Patent 7,083,793 B2; hereafter "Fraser") as evidenced by Landgrebe et al. (Gene 316:47-56, 2003; hereafter "Landgrebe"), Plasmid Vectors (obtained from www.mfa.od.ua/page275.htm, last viewed on 5/9/11), and Dierks (*supra*). This rejection is directed to the cultured sulfatase-producing cell of claims 86-90, 92, and 121 being a *prokaryotic* cell.

The teachings of Fraser and evidentiary references Landgrebe, Plasmid Vectors, and Dierks as applied to claims 101-105, 107, 119, and 123 are set forth above. The difference between Fraser and the invention of claims 86-90, 92, 117, and 121 is that the polypeptide of Fraser has two mismatches relative to SEQ ID NO:2 herein (see Appendix A sequence alignment).

Rosen teaches a polypeptide that is 100% identical to SEQ ID NO:2 herein (see Appendix B sequence alignment) and acknowledges that the polypeptide can be produced using *E. coli* as an expression host and an *E. coli lac* promoter (column 309, line 63 to column 310, line 29), however, does not expressly teach an *E. coli* expression system that uses the *E. coli lac* promoter.

At the time of the invention, it would have been obvious to combine the teachings of Rosen and Fraser to make a BL21(DE3) *E. coli* transformed with an expression vector comprising a polynucleotide encoding the polypeptide of Rosen, which transformant would satisfy the claim limitations as noted above. One would have been motivated to do this because Fraser teaches an *E. coli* expression system that uses the

E. coli lac promoter. One would have had a reasonable expectation of success to make a BL21(DE3) *E. coli* transformed with an expression vector comprising a polynucleotide encoding the polypeptide of Rosen because of the teachings of Rosen and Fraser. Therefore, the cultured sulfatase-producing cell of claims 86-90, 92, 117, and 121 would have been obvious to one of ordinary skill in the art at the time of the invention.

RESPONSE TO ARGUMENT: Beginning at p. 11 of the instant remarks, applicant argues the rejection is obviated by amendment to exclude the claimed cell from being a normal human fibroblast.

Applicant's argument is not found persuasive. At least for the reasons set forth above, it is the examiner's position that Rommerskirch's MLD fibroblast cell infected with a retroviral gene transfer vector comprising a herpes simplex virus thymidine kinase promoter and a sulfatase-encoding nucleic acid is encompassed by the claims.

Conclusion

[20] Status of the claims:

- Claims 86-96, 101-112, and 116-123 are pending.
- Claims 91, 106, and 112 are withdrawn from consideration.
- Claims 86-90, 92-96, 101-105, 107-111, and 116-123 are rejected.
- No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Fri, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/David J. Steadman/
Primary Examiner, Art Unit 1656

APPENDIX A

```
US-10-107-857-15
; Sequence 15, Application US/10107857
; Patent No. 7083793
; GENERAL INFORMATION:
;  APPLICANT: Fraser, Christopher C.
;  TITLE OF INVENTION: SECRETED PROTEINS AND USES THEREOF
;  FILE REFERENCE: 07336-251001
;  CURRENT APPLICATION NUMBER: US/10/107,857
;  CURRENT FILING DATE:  2002-03-26
;  PRIOR APPLICATION NUMBER: 09/514,009
;  PRIOR FILING DATE: 2000-02-25
;  NUMBER OF SEQ ID NOS: 51
;  SOFTWARE: FastSEQ for Windows Version 4.0
; SEQ ID NO 15
;   LENGTH: 374
;   TYPE: PRT
;   ORGANISM: Homo sapiens
US-10-107-857-15

  Query Match             99.7%;  Score 2065;  DB 3;  Length 374;
  Best Local Similarity   99.5%;
  Matches  372;  Conservative    1;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 MAAPALGLVCGRCPELGLVLLLLLLSLLCGAAGSQEAGTGAGAGSLAGSCGCGTPQRPGA 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MAAPALGLVCGRCPELGLVLLLLLLSLLCGAAGSQEAGTGAGAGSLAGSCGCGTPQRPGA 60

Qy         61 HGSSAAAHRYSREANAPGPVPGERQLAHSKMVPIPAGVFTMGTDDPQIKQDGEAPARRVT 120
              ||:|||||||||||||||||||||||||||||| ||||||||||||||||||||||||||
Db         61 HGNSAAAHRYSREANAPGPVPGERQLAHSKMVPIPVGVFTMGTDDPQIKQDGEAPARRVT 120

Qy        121 IDAFYMDAYEVSNTEFEKFVNSTGYLTEAEKFGDSFVFEGMLSEQVKTNIQQAVAAAPWW 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 IDAFYMDAYEVSNTEFEKFVNSTGYLTEAEKFGDSFVFEGMLSEQVKTNIQQAVAAAPWW 180

Qy        181 LPVKGANWRHPEGPDSTILHRPDHPVLHVSWNDAVAYCTWAGKRLPTEAEWEYSCRGGLH 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 LPVKGANWRHPEGPDSTILHRPDHPVLHVSWNDAVAYCTWAGKRLPTEAEWEYSCRGGLH 240

Qy        241 NRLFPWGNKLQPKGQHYANIWQGEFPVTNTGEDGFQGTAPVDAFPPNGYGLYNIVGNAWE 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy        301 WTSDWWTVHHSVEETLNPKGPPSGKDRVKKGGSYMCHRSYCYRYRCAARSQNTPDSSASN 360
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Qy        361 LGFRCAADRLPTMD 374
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APPENDIX B

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US-10-100-683-10571
; Sequence 10571, Application US/10100683
; Patent No. 7368531
; GENERAL INFORMATION:
;  APPLICANT: Rosen, et al.
;  TITLE OF INVENTION: Human Secreted Proteins
;  FILE REFERENCE: PS900
;  CURRENT APPLICATION NUMBER: US/10/100,683
;  CURRENT FILING DATE:  2002-03-19
;  PRIOR APPLICATION NUMBER: US 60/040,162
;  PRIOR FILING DATE: 1997-03-07
;  PRIOR APPLICATION NUMBER: US 60/043,576
;  PRIOR FILING DATE: 1997-04-11
;  PRIOR APPLICATION NUMBER: US 60/047,601
;  PRIOR FILING DATE: 1997-05-23
;  PRIOR APPLICATION NUMBER: US 60/056,845
;  PRIOR FILING DATE: 1997-08-22
;  PRIOR APPLICATION NUMBER: US 60/043,580
;  PRIOR FILING DATE: 1997-04-11
;  PRIOR APPLICATION NUMBER: US 60/047,599
;  PRIOR FILING DATE: 1997-05-23
;  PRIOR APPLICATION NUMBER: US 60/056,664
;  PRIOR FILING DATE: 1997-08-22
;  PRIOR APPLICATION NUMBER: US 60/043,314
;  PRIOR FILING DATE: 1997-04-11
;  PRIOR APPLICATION NUMBER: US 60/047,632
;  PRIOR FILING DATE: 1997-05-23
;  PRIOR APPLICATION NUMBER: US 60/056,892
;  PRIOR FILING DATE: 1997-08-22
;  Remaining Prior Application data removed - See File Wrapper or PALM.
;  NUMBER OF SEQ ID NOS: 13468
;  SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 10571
;   LENGTH: 374
;   TYPE: PRT
;   ORGANISM: Homo sapiens
US-10-100-683-10571

  Query Match           100.0%;  Score 2072;  DB 3;  Length 374;
  Best Local Similarity  100.0%;
  Matches  374;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

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Db          1 MAAPALGLVCGRCPELGLVLLLLLSLLCGAAGSQEAGTGAGAGSLAGSCGCGTPQRPGA 60

Qy         61 HGSSAAAHRYSREANAPGPVPGERQLAHSKMVPIPAGVFTMGTDDPQIKQDGEAPARRVT 120
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Qy        121 IDAFYMDAYEVSNTEFEKFVNSTGYLTEAEKFGDSFVFEGMLSEQVKTNIQQAVAAAPWW 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 IDAFYMDAYEVSNTEFEKFVNSTGYLTEAEKFGDSFVFEGMLSEQVKTNIQQAVAAAPWW 180

Qy        181 LPVKGANWRHPEGPDSTILHRPDHPVLHVSWNDAVAYCTWAGKRLPTEAEWEYSCRGGLH 240
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Db        181 LPVKGANWRHPEGPDSTILHRPDHPVLHVSWNDAVAYCTWAGKRLPTEAEWEYSCRGGLH 240

Qy        241 NRLFPWGNKLQPKGQHYANIWQGEFPVTNTGEDGFQGTAPVDAFPPNGYGLYNIVGNAWE 300
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Qy        301 WTSDWWTVHHSVEETLNPKGPPSGKDRVKKGGSYMCHRSYCYRYRCAARSQNTPDSSASN 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 WTSDWWTVHHSVEETLNPKGPPSGKDRVKKGGSYMCHRSYCYRYRCAARSQNTPDSSASN 360

Qy        361 LGFRCAADRLPTMD 374
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Db        361 LGFRCAADRLPTMD 374
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